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L4: Entry 2 of 2 File: DWPI Aug 14, 1997

DERWENT-ACC-NO: 1997-427773
DERWENT-WEEK: 200254

TITLE: Nucleic acid encoding new potassium channel designated TWIK-1 - useful for treating channel deficiency diseases, screening for active agents and for diagnosis

Basic Abstract Text (2):
USE - (II) is the first member of a new family of channels consisting of 4 transmembrane segments and two P domains, and being only weakly rectifying. (I), vectors, the cells of (2) and (II) are used to compensate for deficiency of potassium channels in various tissues. Modulators identified by method (3) may also be useful therapeutically, e.g. for control of epilepsy, arrhythmia, vascular disease, neurodegeneration (particularly of ischaemic or anoxic origin), endocrine or muscular disorders. (I) and the vectors can also be used to create transgenic animals (especially knock-out animals) for use as models of TWIK-1 related diseases. Analysis of the sequence of the TWIK-1 gene may be used for pre-natal diagnosis of disease. Ab can be used to detect TWIK-1 channels and for inhibiting or activating the channels in vivo.

Equivalent Abstract Text (2):
USE - (II) is the first member of a new family of channels consisting of 4 transmembrane segments and two P domains, and being only weakly rectifying. (I), vectors, the cells of (2) and (II) are used to compensate for deficiency of potassium channels in various tissues. Modulators identified by method (3) may also be useful therapeutically, e.g. for control of epilepsy, arrhythmia, vascular disease, neurodegeneration (particularly of ischaemic or anoxic origin), endocrine or muscular disorders. (I) and the vectors can also be used to create transgenic animals (especially knock-out animals) for use as models of TWIK-1 related diseases. Analysis of the sequence of the TWIK-1 gene may be used for pre-natal diagnosis of disease. Ab can be used to detect TWIK-1 channels and for inhibiting or activating the channels in vivo.

Equivalent Abstract Text (4):
USE - (II) is the first member of a new family of channels consisting of 4 transmembrane segments and two P domains, and being only weakly rectifying. (I), vectors, the cells of (2) and (II) are used to compensate for deficiency of potassium channels in various tissues. Modulators identified by method (3) may also be useful therapeutically, e.g. for control of epilepsy, arrhythmia, vascular disease, neurodegeneration (particularly of ischaemic or anoxic origin), endocrine or muscular disorders. (I) and the vectors can also be used to create transgenic animals (especially knock-out animals) for use as models of TWIK-1 related diseases. Analysis of the sequence of the TWIK-1 gene may be used for pre-natal diagnosis of disease. Ab can be used to detect TWIK-1 channels and for inhibiting or activating the channels in vivo.

Equivalent Abstract Text (6):
USE - (II) is the first member of a new family of channels consisting of 4 transmembrane segments and two P domains, and being only weakly rectifying. (I), vectors, the cells of (2) and (II) are used to compensate for deficiency of potassium channels in various tissues. Modulators identified by method (3) may also be useful therapeutically, e.g. for control of epilepsy, arrhythmia, vascular disease,

neurodegeneration (particularly of ischaemic or anoxic origin), endocrine or muscular disorders. (I) and the vectors can also be used to create transgenic animals (especially knock-out animals) for use as models of TWIK-1 related diseases. Analysis of the sequence of the TWIK-1 gene may be used for pre-natal diagnosis of disease. Ab can be used to detect TWIK-1 channels and for inhibiting or activating the channels in vivo.

Equivalent Abstract Text (8):
USE - (II) is the first member of a new family of channels consisting of 4 transmembrane segments and two P domains, and being only weakly rectifying. (I), vectors, the cells of (2) and (II) are used to compensate for deficiency of potassium channels in various tissues. Modulators identified by method (3) may also be useful therapeutically, e.g. for control of epilepsy, arrhythmia, vascular disease, neurodegeneration (particularly of ischaemic or anoxic origin), endocrine or muscular disorders. (I) and the vectors can also be used to create transgenic animals (especially knock-out animals) for use as models of TWIK-1 related diseases. Analysis of the sequence of the TWIK-1 gene may be used for pre-natal diagnosis of disease. Ab can be used to detect TWIK-1 channels and for inhibiting or activating the channels in vivo.

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L2: Entry 1 of 1 File: USPT Jan 11, 2000

US-PAT-NO: 6013470
DOCUMENT-IDENTIFIER: US 6013470 A

TITLE: Family of mammalian potassium channels, their cloning and their use especially for the screening of drugs

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lesage; Florian	Nice			FR
Guillemare; Eric	Nice			FR
Fink; Michel	Cannes La Bocca			FR
Duprat; Fabrice	Valluris			FR
Lazdunski; Michel	Nice			FR
Romey; Georges	Nice			FR
Barhanin; Jacques	Nice			FR

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 536/23.1

CLAIMS:

We claim:

1. An isolated and purified nucleic acid molecule encoding a mammalian protein which comprises 2 P domains and 4 transmembrane segments, and is competent to transport potassium across a membrane.

2. An isolated and purified nucleic acid molecule encoding a human protein which comprises 2 P domains and 4 transmembrane segments, and is competent to transport potassium across a membrane.

3. The nucleic acid molecule of claim 2 encoding a human protein which exhibits weak inward rectification.

4. The nucleic acid molecule of claim 3 which is expressed in brain and heart tissue and in addition, in at least one of the following tissues: placenta, liver, skeletal, muscle, kidney and pancreas.

5. The human nucleic acid sequence of claim 2 which comprises the sequence represented by SEQ ID No. 1.

6. A self replication vector comprising the nucleic acid molecule of claim 2.

7. A cell transformed with the self replicating vector of claim 6, which cell expresses a human protein which comprises 2 P domains and 4 transmembrane segments, and is competent to transport potassium across a membrane.

8. A micro-injected cell comprising the RNA transcript synthesized from the nucleic acid molecule of claim 2, which cell expresses a human protein which comprises 2 P domains and 4 transmembrane segments, and is competent to transport

potassium across a membrane.

9. The transformed cell of claim 7, which cell is selected from the group consisting of prokaryotes and eukaryotes.

10. The transformed cell of claim 9 which is a bacterium.

11. The transformed cell of claim 10 which is a yeast, insect, plant or mammalian cell.

12. A method for the production of a human protein competent to transport potassium across a membrane which comprises 2 P domains and 4 transmembrane segments, comprising transferring the vector of claim 6 into a cellular host, culturing the cellular host under conditions allowing the production of said potassium channel, and purifying the human potassium channel.

13. The method of claim 12 wherein the cellular host is selected from the group consisting of prokaryotes and eukaryotes.

14. A pharmaceutical composition for the compensation of a deficiency in potassium channels at the level of one or more tissues, which comprises an isolated and purified nucleic acid molecule encoding a human protein comprising 2 P domains and 4 transmembrane segments which protein is competent to transport potassium across a membrane.

15. A pharmaceutical composition which comprises human cells transformed with the nucleic acid molecule of claim 2.

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L1: Entry 1 of 1 File: USPT Oct 30, 2001

US-PAT-NO: 6309855
DOCUMENT-IDENTIFIER: US 6309855 B1

TITLE: Family of mammalian potassium channels, their cloning and their use, especially for the screening of drugs

DATE-ISSUED: October 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Duprat; Fabrice	Vallauris			FR
Lesage; Florian	Paris			FR
Fink; Michel	La Bocca			FR
Lazdunski; Michel	Nice			FR

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 514/44, 536/23.1, 536/23.4, 536/23.5, 536/24.1

CLAIMS:

What is claimed is:

1. An isolated and purified nucleic acid molecule coding for a protein capable of forming a potassium (K.sup.+) ion channel, comprising two P domains and three or four transmembrane segments.

2. The nucleic acid molecule of claim 1 coding for a protein wherein the number of P domains is two and the number of transmembrane segments is four.

3. The nucleic acid molecule of claim 1 which is human.

4. The nucleic acid molecule of claim 1 which is a cDNA copy of a 2.6 kilobase transcript expressed at high levels in the pancreas and placenta, and at lower levels in the brain, lung, prostate, heart, kidney, uterus small intestine and colon.

5. The nucleic acid sequence of claim 1 which codes for a protein which comprises the sequence represented by SEQ ID NO:4.

6. The isolated and purified nucleic acid sequence of claim 1 which codes for a protein which comprises the sequence represented by SEQ ID NO:4 or a sequence having the equivalent function of being capable of forming a potassium (K.sup.+) ion channel which comprises two P domains and four transmembrane segments.

7. An isolated and purified nucleic acid sequence of claim 2 which comprises an open reading frame (ORF) of 1185 nucleotides.

8. The isolated and purified nucleic acid sequence of claim 7 which is human.

9. A self replicating vector comprising the nucleic acid molecule of claim 1.

10. A cell transformed with the vector of claim 9, which cell is selected from the

group consisting of prokaryotes and eukaryotes.

11. The transformed cell of claim 10 which is a yeast, insect cell, plant cell or mammalian cell.

12. The transformed cell of claim 10 which is a bacterium.

13. A method for the expression and isolation of a potassium transport channel encoded by a nucleic acid molecule according to claim 1 in a competent host cell comprising transferring a self-replicating vector including said nucleic acid molecule into a competent host cell, culturing said host cell under conditions allowing the production of the potassium transport channel, and isolating and purifying the polypeptide comprising the potassium transport channel.